Vacuum soft lithography to direct neuronal polarization

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Public Summary:
Individual nerve cells, or neurons, grow long thin outgrowths (axons and dendrites) that form the connections of nervous system. These connections are governed by a complex set of “instructions” or guidance molecules which either promote or inhibit the directional growth of the connecting fibers. Ultimately, the use of stem cells to replace or repair connections in the human nervous system will require detailed information on how individual neurons connect. This information would then be used to guide new neurons to integrate into the existing circuitry in a way that restores rather than hinders circuit function in patients. Although it has been possible to test one molecule at a time and determine how a neuron responds, it has challenging to test how axons and dendrites respond to more complex patterns of molecules. This manuscript describes a successful bioengineering strategy for guiding the directional growth of nerve cell connection on a solid state chip. The advance described here is the ability to “print” many molecules is precisely defined patterns in a single step. The ability to test a neuron’s response to a complex set of instructions will accelerate the development of stem cell therapies for the nervous system as well as lead the way for designing prosthetic computer devices that can effectively communicate with neurons in the human nervous system.

Scientific Abstract:
The ability to coat surfaces with pre-determined patterns of biomolecules by soft lithography has found use in areas ranging from fundamental biology to translational medicine, such as tissue engineering and diagnostics. However, existing surface patterning techniques (e.g., microcontact printing and traditional lithography) are unable to pattern several biomolecules in a single step. Here we introduce a simple method to simultaneously pattern multiple biomolecules in complex two-dimensional configurations onto substrates with better than 2 μm resolution. This protocol, termed vacuum soft lithography, utilized below ambient pressures temporarily stored within a removable microfluidic template to expose specific regions of a substrate to multiple biochemical solutions. We demonstrate the utility of this vacuum soft lithography technique by fabricating a multi-component array that directs the adhesion, polarization, and neurite guidance of primary hippocampal neurons.